IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor: Stephen A. Mamchur	Art Unit: 1616
Filing Date: September 22, 2003	Examiner: Nathan W. Schlientz, Ph.D.
Serial No: 10/668,075	
Docket: 025357.001; 097928-0001	
Title: A SYSTEM FOR USE BY COMPOUNDING PHARMACISTS TO PRODUCE HORMONE REPLACEMENT MEDICINE CUSTOMIZED FOR EACH CONSUMER	

DECLARATION UNDER 37 CFR § 1.132
STEPHEN A. MAMCHUR

Commissioner for Patents
Alexandria VA 22313

I, STEPHEN MAMCHUR, do hereby declare as follows:

I am sole inventor of the invention described and claimed in this patent application. I have a background in pharmaceutical chemistry and processing, and own a pharmacy located in Calgary, Alberta.

I understand the Examiner has questioned whether the invention I am claiming in my application is new with respect to pharmaceutical processing methodology described in patent publications by Chiang (WO 90/11064), Rosenbaum (U.S. Patent 5,709,878), Carrara (WO 02/11768), and Muni (U.S. Patent 6,708,822).

Developing the Invention

Bioidentical hormone replacement (BHR) therapy is being increasingly recognized for its therapeutic value in managing a number of clinical conditions. However, for optimal effect, it is important that the pharmaceutical composition be tailored to the needs of each consumer. In this way, they may receive optimal supplementation of the hormones which they need, but not the hormones their body makes in proper amounts (which, if over-administered, could increase the risk of cancer).

Until the making of my invention, it was difficult for the consumer to get such tailor-made BHR products. Using previous technology, the making of customized BHR products required careful weighing of hormone powders and compounding them into suitable excipients using special equipment, clothing, and air filters. This is described in the Background section of my patent application (paragraphs [0009] to [0014] of US 2004/0180866 A1). Producing BHR products in this way was clearly outside the capabilities of the ordinary pharmacy, and was generally not worth the trouble and expense of the few compounding pharmacies located in major urban centers.

I decided that a system of concentrated pre-dissolved reagent compositions would be better for making customized BHR products. The retail pharmacist would measure out the appropriate amounts of the liquid hormone reagents required for a particular consumer. This could be done by a pharmaceutical assistant of ordinary competence at an ordinary pharmacy, since it does not require special equipment or techniques.

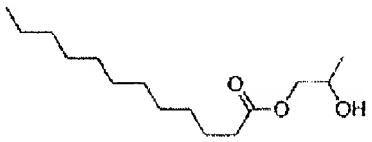
In developing this invention, there were some technical challenges to overcome. Making concentrated reagent solutions for estrogen hormones was a challenge, because estrogens were known not to be highly soluble in the usual pharmaceutically compatible solvents. What I needed was a series of different estrogen reagent compositions that were sufficiently concentrated so that they would be therapeutically effective once diluted with other reagents in the preparation of a customized BHR product.

As described in paragraph [0160] of my patent application, I discovered that combining ethoxy diglycol and propylene glycol yields a solvent that dissolves estrogen hormones at the concentrations that I needed. Now that such concentrated estrogen reagents have been obtained, someone reading my patent will understand that further testing may lead to concentrated estrogen reagents using other solvent combinations.

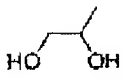
Chiang, Rosenbaum, and Carrara technology

The Chiang, Rosenbaum, and Carrara references focus on making final products. Chiang describes skin products made with a particular combination of permeation enhancers. Rosenbaum describes skin creams containing phospholipids. Carrara describes skin products or suppositories made with long-chain alcohols. They are not intended to provide retail pharmacists with reagent systems like those referred to in my patent application.

The compositions described by Chiang are made with a diethylene glycol either in combination with propylene glycol *monolaurate*. The structure of propylene glycol monolaurate is $C_{15}H_{30}O_3$, which has the following structure:



Contrast this with the structure of simple propylene glycol ($C_3H_8O_2$) referred to in claim 123 of my patent application:



The fatty acid side chain on propylene glycol monolaurate gives it considerably different physicochemical properties, both in its ability to dissolve active ingredients, and in its function as an excipient.

Muni technology

The Muni patent refers to kits for compounding pharmaceuticals, but it is not set up to provide custom-tailored products. Their technology is aimed at providing a kit where a predetermined amount of active ingredient is combined with a predetermined amount of excipient by the pharmacist. What results is a stockpile of product at a particular predetermined dosage that the pharmacist puts on the shelf, to be dispensed at a later time when someone comes into the store with a prescription for that dosage. This is quite different from my invention, where the pharmacist makes the product only after receiving the prescription, measuring out a variable amount of hormone for each patient before compounding the product.

The Muni patent is indicated as being assigned to *CutisPharma*. Enclosed with this Declaration is information downloaded from the *CutisPharma* website about their FiRXst™ line of products. The information from the website confirms the nature of the technology described in the Muni patent. In their kits for making progesterone suppositories, the hormone is supplied as a solid. In their kits for making hydrocortisone ultrasound gel, the hormone is supplied as a suspension (not a solution). In their kits for making testosterone in petrolatum (Vaseline®), the hormone is supplied in solution.

There is no indication that the hormone reagent in any of these kits can be combined with another hormone reagent to make a pharmaceutical composition. In fact, all of the products are made by combining the entire single hormone component of the kit with the entire excipients component. There is no indication that the amount of the hormone solution can be diluted or combined with other reagents in accordance with the needs of the individual consumer. In fact, five different kits are sold for producing products with different doses of progesterone.

In addition, there is no product in the FiRXst line described on the website that contains estrogen. Estrogens are used in the Muni patent in combination with *lactose* (Example 7; claim 18). Of course, lactose is a solid, and is combined with powdered estrogen as a solid excipient to make it easier to weigh out. Muni does not instruct the reader to prepare a concentrated solution of estrogen as a reagent, or for any other purpose.

Clearly, the Muni system has a different focus, involving differently apportioned ingredients that are used in a different way.

Recognition of Commercial Importance

The value of customized hormone replacement was discussed on the Oprah Winfrey Show in January of this year. The therapeutic and commercial potential of my invention has been recognized in the industry. The invention was a finalist in the Saskatchewan BioVenture Challenge in 2007. It was also the winner the same year in Saskatchewan's business plan competition for young entrepreneurs ("My Future is Here").

Conclusion

None of the references cited in the Office Action suggest that active ingredients should be prepared as concentrated reagents, and then measured out in different amounts for each consumer. None of the references suggest that multiple concentrated reagents containing different hormones can be combined together based on a consumer's particular needs.

My system is new and different. For the first time, ordinary pharmacies can provide BHR products that are customized for their customers. Issuing this patent will help me get large investors to commercialize the invention for the benefit of consumers throughout the U.S.

I hereby declare that all statements made in this Declaration of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Dec 18/09
Date

Stephen A. Mamchur, Pharm.D., J.D.
Calgary, Alberta, Canada

Enclosures:

- Information obtained from *CutisPharma* website
- Article from *Prince Albert Herald* regarding BioVenture award

CUTISPHARMA, INC.

SMART PRODUCTS FOR SMART PEOPLE™

FIRST™— HYDROCORTISONE

FIRST™— MOUTHWASH BLM

FIRST™— PROGESTERONE

- **VGS 25**
- **VGS 50**
- **VGS 100**
- **VGS 200**
- **VGS 400**

FIRST™— TESTOSTERONE

FIRST™— TESTOSTERONE MC

FIRST™-

Unit-of-Use Prescription Compounding Kits

Fast and Easy to use

Pre-measured and Pre-weighed
Facilitates Reimbursement
Compound While Customer Waits

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27

FIRST™- Progesterone VGS 25 ℞

25 mg Progesterone Vaginal Suppository USP Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

Each FIRST™- Progesterone VGS 25 Compounding Kit is comprised of 0.75 grams of wettable progesterone USP powder and 68.25 grams of fatty acid base (hard fat NF).* FIRST™- Progesterone VGS 25 Compounding Kit also contains the following components necessary to prepare 30 suppositories: 30-unit suppository mold w/caps, stirrer, suppository filling tool, guide plate, and 30-unit suppository mold protective cover w/suppository dispensing tool attached.

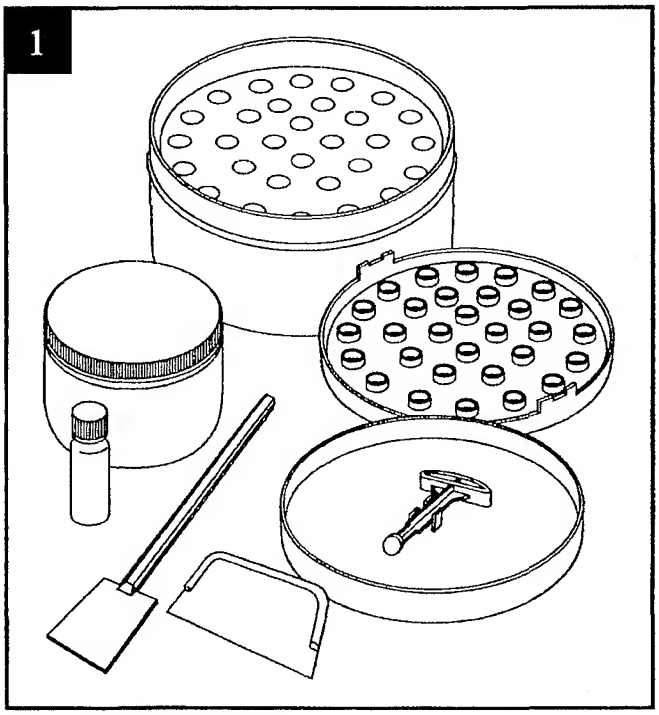
How Supplied and Compounding Directions

Size	30 Suppositories
NDC#	65628-060-01
Progesterone USP	0.75 g
Fatty Acid Base (Hard Fat NF)	68.25 g

TO THE PHARMACIST

Everything you need to make this ℞ is included...

1

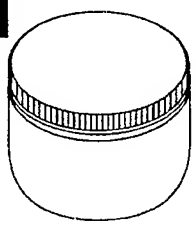


1

PROGESTERONE BOTTLE

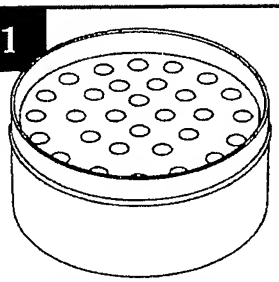
1. FIRST™- Progesterone VGS 25 Compounding Kit contains pre-weighed progesterone powder and pre-weighed fatty acid base in sufficient quantity for the pharmacist to prepare 30 vaginal suppositories, each containing 25 mg of progesterone. ***Important*** - Prior to compounding and dispensing, read the instructions completely and make certain that all the components are present.

1



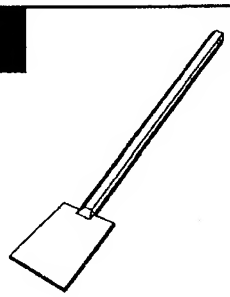
FATTY ACID BASE JAR

1



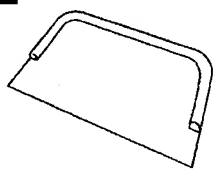
30-UNIT SUPPOSITORY MOLD W/CAPS

1



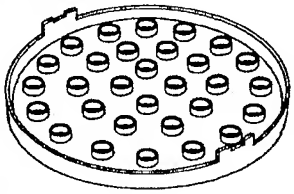
STIRRER

1



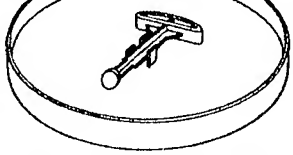
SUPPOSITORY FILLING TOOL

1



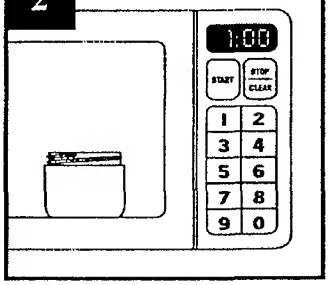
GUIDE PLATE

1



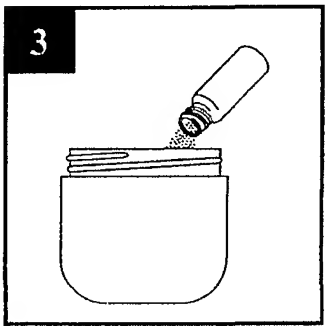
30-UNIT SUPPOSITORY MOLD COVER W/ SUPPOSITORY DISPENSING TOOL ATTACHED

2

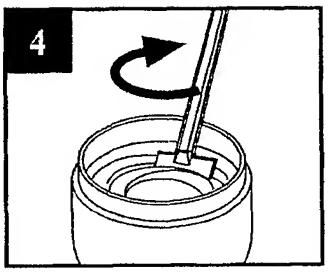


2. Remove the cap from jar containing fatty acid base and melt the base placing the jar in a standard microwave. ***Melting times may vary depending on the type of microwave used.*** It is recommended that you initially set the timer for 1 minute and check to see if the base has melted. If it has not, return the jar of base to the microwave for 15 second increments until the base is ***completely*** melted. Generally, the fatty acid base will completely melt between 1 and 3 minutes. DO NOT OVERHEAT.

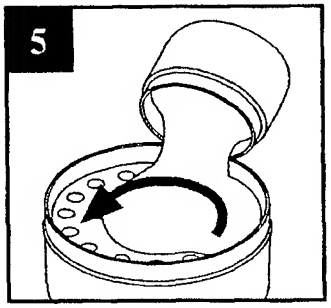
3



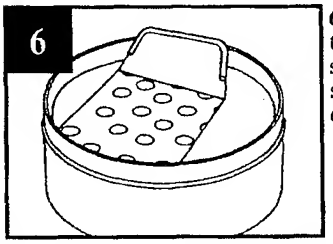
3. Tap the top and bottom of the bottle to loosen the progesterone powder and remove the cap. Empty the entire contents of the bottle into the jar containing the melted fatty acid base. It is recommended that you also tap the bottom and sides of the bottle while emptying. The appropriate quantity of progesterone powder has been packaged in the bottle to deliver enough progesterone to provide 25 mg for each suppository.



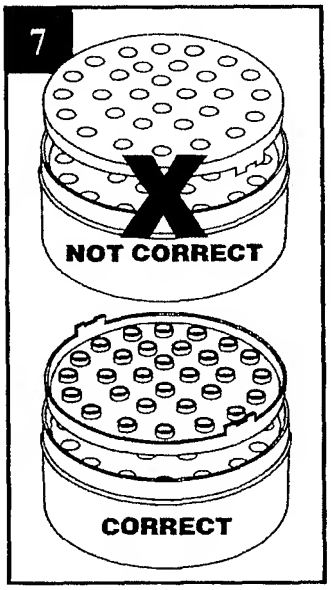
4. Using the stirrer provided, carefully stir the progesterone powder in the melted fatty acid base until an homogeneous suspension is apparent (30 to 60 seconds). ***Be careful not to stir so vigorously as to spill the suspension outside the jar.***



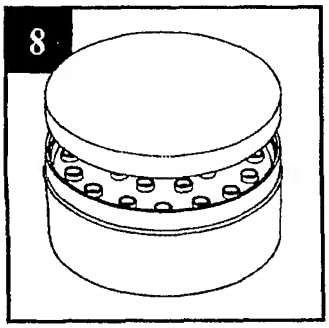
5. With an even flow, carefully pour the entire suspension from the jar onto the 30-unit suppository mold in a circular motion filling each of the 30 suppository cavities.



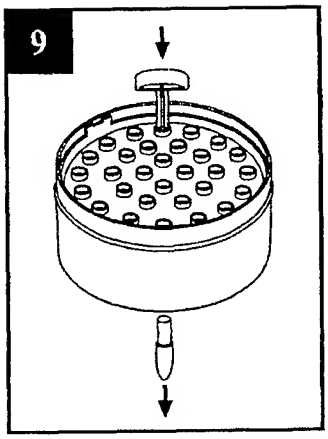
6. Using the suppository filling tool provided, spread the suspension evenly over the suppository cavities until all the cavities are completely filled.



7. Place the provided guide plate onto the mold with the 30 raised guide holes facing upward. Make certain the notches on the guide plate align with notches on suppository mold. This will ensure that the 30 suppository cavities are aligned with the raised holes in the guide plate. Gently push the guide plate down to lock it in place. It is important that you fit the guide plate properly in order for your patient to dispense the suppositories easily.



8. Place the provided cover with attached suppository dispensing tool onto the suppository mold. Store entire unit at refrigerated temperature for at least 15 minutes in order to allow the suppositories to solidify. Visually check the suppositories for solidification before dispensing the entire unit to your patient.



9. Make certain to instruct your patient how to dispense each suppository for daily use. Using the suppository dispensing tool attached to the mold cover, place the tip of the tool into the guide plate and with a firm force push the suppository through. Your patient should refrigerate the mold at least 1 hour for total solidification before dispensing the first suppository for use. ***Important: Be sure to instruct your patient to remove the red suppository cap from the suppository before inserting each suppository.***

Prior to compounding, store FIRST™- Progesterone VGS 25 Compounding Kit at room temperature between 15°-30°C (59°-86°F) [see USP]. Also, store the compounded suppositories in the 30-unit suppository mold in the refrigerator (2°-8°C [36°-46°F]). FIRST™- Progesterone VGS 25 Compounding Kit components have a two-year expiration date.** The preparation of vaginal suppositories using FIRST™- Progesterone VGS 25 Compounding Kit complies with the requirements of USP, and as such, compounded suppositories made using FIRST™- Progesterone VGS 25 Compounding Kit can be used for up to ninety days after the day on which they were compounded.

When compounded and dispensed according to the instructions, average suppository weight has been found to be 2.3 grams and contain 90–110% of progesterone as labeled.**

The suppository mold and its accessories contained in this kit meet the requirements for USP Cytotoxicity Test, as well as Class VI Tests for plastic containers.**

Instruct patient as follows:
- For vaginal use only
- Do not take orally
- Do not insert in urinary opening or anus
- Avoid contact with eyes
- Keep out of reach of children
- Protect from light
- Keep container tightly closed
- Store suppositories in the mold, in the refrigerator
- Remove red caps from suppositories prior to use

* Certificate of analysis on file

** Data and documentation on file

℞ only

Issued: June 2006

U.S. Patents Pending

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SUPPOSITORY

FIRST™- Progesterone VGS 400 R

400 mg Progesterone Vaginal Suppository USP Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

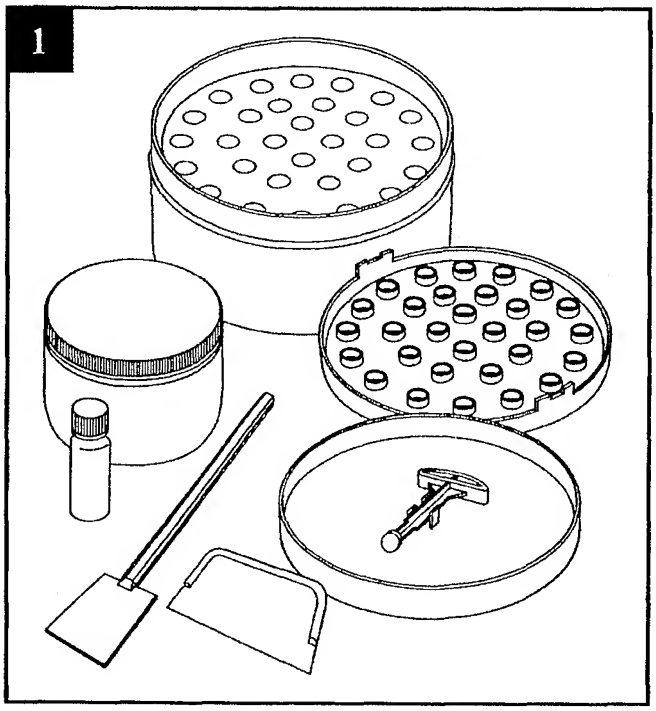
Each FIRST™- Progesterone VGS 400 Compounding Kit is comprised of 12.0 grams of wettable progesterone USP powder and 57.0 grams of fatty acid base (hard fat NF).* FIRST™- Progesterone VGS 400 Compounding Kit also contains the following components necessary to prepare 30 suppositories: 30-unit suppository mold w/caps, stirrer, suppository filling tool, guide plate, and 30-unit suppository mold protective cover w/suppository dispensing tool attached.

How Supplied and Compounding Directions

Size	30 Suppositories
NDC#	65628-064-01
Progesterone USP	12.0 g
Fatty Acid Base (Hard Fat NF)	57.0 g

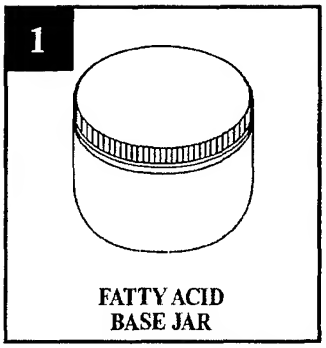
TO THE PHARMACIST

Everything you need to make this R is included...

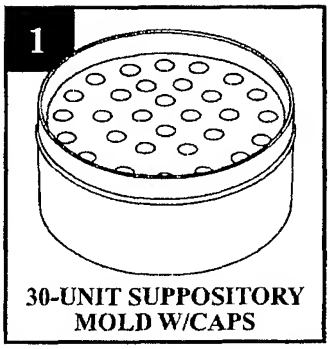


PROGESTERONE BOTTLE

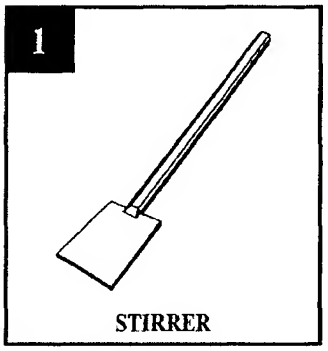
1. FIRST™- Progesterone VGS 400 Compounding Kit contains pre-weighed progesterone powder and pre-weighed fatty acid base in sufficient quantity for the pharmacist to prepare 30 vaginal suppositories, each containing 400 mg of progesterone. ***Important*** - Prior to compounding and dispensing, read the instructions completely and make certain that all the components are present.



FATTY ACID BASE JAR

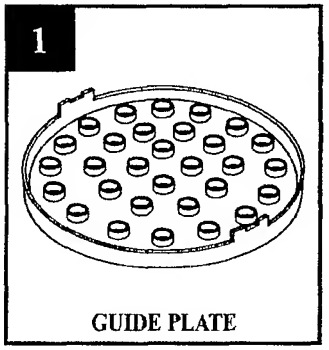


30-UNIT SUPPOSITORY MOLD W/CAPS



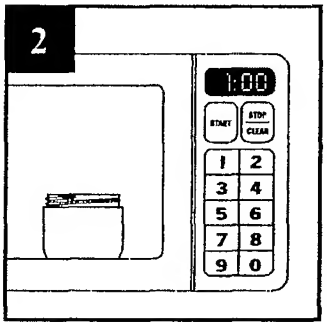
STIRRER

SUPPOSITORY FILLING TOOL

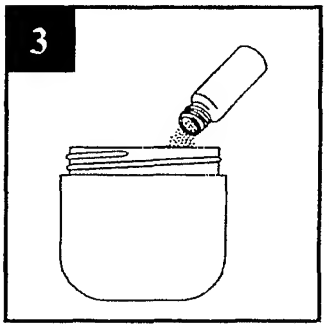


GUIDE PLATE

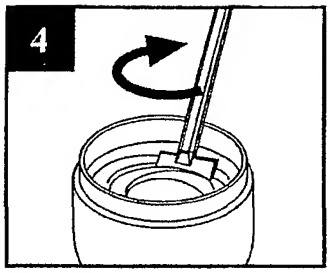
30-UNIT SUPPOSITORY MOLD COVER W/ SUPPOSITORY DISPENSING TOOL ATTACHED



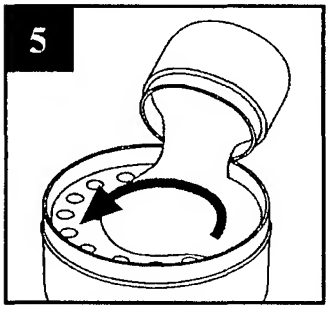
2. Remove the cap from jar containing fatty acid base and melt the base placing the jar in a standard microwave. ***Melting times may vary depending on the type of microwave used.*** It is recommended that you initially set the timer for 1 minute and check to see if the base has melted. If it has not, return the jar of base to the microwave for 15 second increments until the base is ***completely*** melted. Generally, the fatty acid base will completely melt between 1 and 3 minutes. DO NOT OVERHEAT.



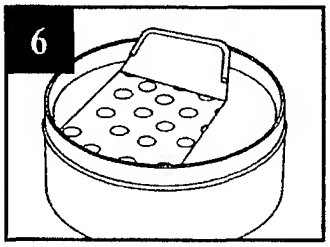
3. Tap the top and bottom of the bottle to loosen the progesterone powder and remove the cap. Empty the entire contents of the bottle into the jar containing the melted fatty acid base. It is recommended that you also tap the bottom and sides of the bottle while emptying. The appropriate quantity of progesterone powder has been packaged in the bottle to deliver enough progesterone to provide 400 mg for each suppository.



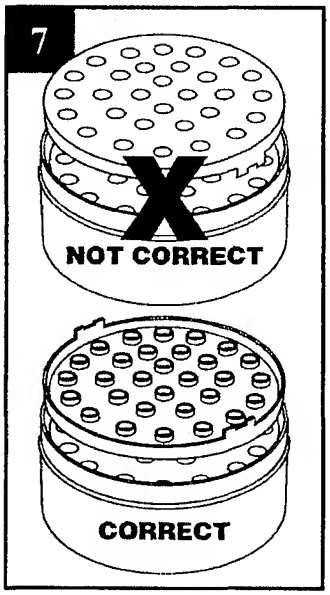
4. Using the stirrer provided, carefully stir the progesterone powder in the melted fatty acid base until an homogeneous suspension is apparent (60 to 90 seconds). ***Be careful not to stir so vigorously as to spill the suspension outside the jar.***



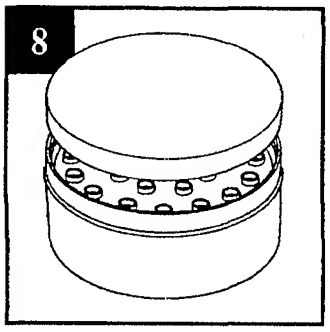
5. With an even flow, carefully pour the entire suspension from the jar onto the 30-unit suppository mold in a circular motion filling each of the 30 suppository cavities.



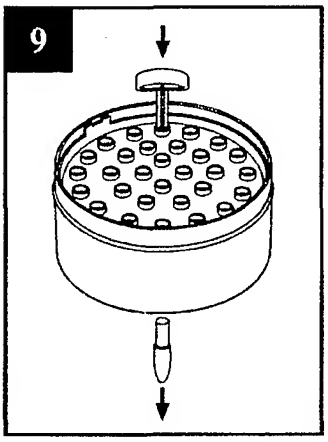
6. Using the suppository filling tool provided, spread the suspension evenly over the suppository cavities until all the cavities are completely filled.



7. Place the provided guide plate onto the mold with the 30 raised guide holes facing upward. Make certain the notches on the guide plate align with notches on suppository mold. This will ensure that the 30 suppository cavities are aligned with the raised holes in the guide plate. Gently push the guide plate down to lock it in place. It is important that you fit the guide plate properly in order for your patient to dispense the suppositories easily.



8. Place the provided cover with attached suppository dispensing tool onto the suppository mold. Store entire unit at refrigerated temperature for at least 15 minutes in order to allow the suppositories to solidify. Visually check the suppositories for solidification before dispensing the entire unit to your patient.



9. Make certain to instruct your patient how to dispense each suppository for daily use. Using the suppository dispensing tool attached to the mold cover, place the tip of the tool into the guide plate and with a firm force push the suppository through. Your patient should refrigerate the mold at least 1 hour for total solidification before dispensing the first suppository for use. ***Important: Be sure to instruct your patient to remove the red suppository cap from the suppository before inserting each suppository.***

Prior to compounding, store FIRST™- Progesterone VGS 400 Compounding Kit at room temperature between 15°-30°C (59°-86°F) [see USP]. Also, store the compounded suppositories in the 30-unit suppository mold in the refrigerator (2°-8°C [36°-46°F]). FIRST™- Progesterone VGS 400 Compounding Kit components have a two-year expiration date.** The preparation of vaginal suppositories using FIRST™- Progesterone VGS 400 Compounding Kit complies with the requirements of USP, and as such, compounded suppositories made using FIRST™- Progesterone VGS 400 Compounding Kit can be used for up to ninety days after the day on which they were compounded.

When compounded and dispensed according to the instructions, average suppository weight has been found to be 2.3 grams and contain 90–110% of progesterone as labeled.**

The suppository mold and its accessories contained in this kit meet the requirements for USP Cytotoxicity Test, as well as Class VI Tests for plastic containers.**

Instruct patient as follows:
- For vaginal use only
- Do not take orally
- Do not insert in urinary opening or anus
- Avoid contact with eyes
- Keep out of reach of children
- Protect from light
- Keep container tightly closed
- Store suppositories in the mold, in the refrigerator
- Remove red caps from suppositories prior to use

* Certificate of analysis on file

** Data and documentation on file

℞ only

Issued: June 2006

U.S. Patents Pending

Distributed By:

CUTISPHARMA, INC.

SMART PRODUCTS FOR SMART PEOPLE™

Beverly, MA 01915, USA www.cutispharma.com

FIRST®-Testosterone ℞

2% Testosterone in White Petrolatum Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

Each FIRST®- Testosterone in White Petrolatum Compounding Kit contains 1.4312 grams of micronized testosterone propionate USP (100 mg testosterone per mL) in solution* (total volume: 12 mL) with sesame oil NF, butylated hydroxytoluene NF, and benzyl alcohol NF.

FIRST®- Testosterone in White Petrolatum Compounding Kit also contains 48 grams of white petrolatum for topical use. When compounded, the final product provides an homogeneous formulation containing 2% testosterone.

How Supplied and Compounding Directions

Size (Net Weight)	60 grams
NDC#	65628-020-01
Testosterone Solution	12 mL (100 mg/mL)
White Petrolatum	48 grams

One 5 mL teaspoonful is approximately equivalent to 5.3 gm of compounded product containing equivalent of 106 mg of testosterone.

TO THE PHARMACIST

Everything you need to make this Rx is included...

1. FIRST®- Testosterone in White Petrolatum Compounding Kit contains pre-weighed white petrolatum in a mixing jar, pre-measured testosterone solution, and a stirrer.

2. **Important** - Prior to dispensing, pour the entire contents of the bottle containing testosterone propionate in oil into white petrolatum.

3. Stir gently until homogeneous in appearance (2 to 3 minutes).

Prior to compounding, store FIRST®- Testosterone in White Petrolatum Compounding Kit at room temperature between 15°-30°C (59°-86°F). Also store final formulation at room temperature, 15°-30°C (59°-86°F).

FIRST®- Testosterone in White Petrolatum Compounding Kit components have a three-year expiration date.** Based on real time controlled room temperature and humidity testing, *compounded* FIRST®- Testosterone in White Petrolatum is stable for at least six months.**

Each lot of FIRST®- Testosterone solution meets USP Microbial Limit Tests <61>** for the absence of USP designated pathogens, as well as not more than 100 CFU/mL for total bacterial count and for total yeast and mold. FIRST®- Testosterone solution also meets USP Antimicrobial Effectiveness Testing <51>**. Antimicrobial effectiveness has been demonstrated in freshly prepared testosterone propionate solution samples and testosterone propionate solution samples stored at accelerated ICH storage conditions (40±2°C/75%RH).

For external use only. Avoid contact with eyes. Keep container tightly closed. Keep out of the reach of children. Compounded product, as dispensed, is ***stable for at least 180 days*** at room temperature.

* Certificate of analysis on file

** Data and documentation on file

℞ ONLY

Revised: March 2008
U.S. Patent No. 6,708,822 B1
Additional U.S. Patent Pending

Distributed By:
CUTISPHARMA, INC.
SMART PRODUCTS FOR SMART PEOPLE™
Woburn, MA 01801, USA www.cutispharma.com

TOPICAL

FIRST®- Testosterone MC ℞

2% Testosterone MC in Moisturizing Cream Base Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

Each FIRST®- Testosterone MC in Moisturizing Cream Base Compounding Kit contains 1.4312 grams of micronized testosterone propionate USP (100 mg testosterone per mL) in solution* (total volume: 12 mL) with sesame oil NF, butylated hydroxytoluene NF, and benzyl alcohol NF.

FIRST®- Testosterone MC in Moisturizing Cream Base Compounding Kit also contains 48 grams of Moisturizing Cream Base for topical use. When compounded, the final product provides an homogeneous formulation containing 2% testosterone.

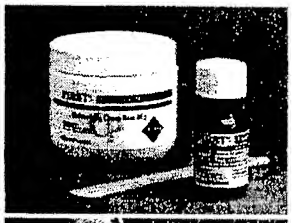
How Supplied and Compounding Directions

Size (Net Weight)	60 grams
NDC#	65628-021-01
Testosterone Solution	12 mL (100 mg/mL)
Moisturizing Cream Base	48 grams

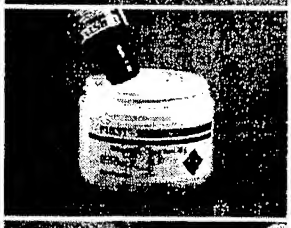
One 5 mL teaspoonful is approximately equivalent to 6.1 gm of compounded product containing equivalent of 122 mg of testosterone.

TO THE PHARMACIST

Everything you need to make this ℞ is included...

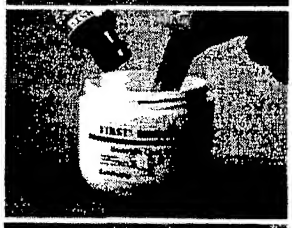


1. FIRST®- Testosterone MC in Moisturizing Cream Base Compounding Kit contains pre-weighed moisturizing cream base in a mixing jar, pre-measured testosterone solution, and a stirrer.



2. **Important - Be careful not to spill the contents while mixing.** Prior to dispensing, pour a few drops of the testosterone propionate in oil into moisturizing cream base.

3. Mix well to wet the base.



4. Continue to gradually add testosterone propionate in oil into moisturizing cream base and mix until all of the testosterone propionate in oil has been added to the moisturizing cream base

5 Continue stirring until homogeneous in appearance (2 to 3 minutes).

Prior to compounding, store FIRST®- Testosterone MC in Moisturizing Cream Base Compounding Kit at room temperature between 15°-30°C (59°-86°F). Also store final formulation at room temperature, 15°-30°C (59°-86°F).

FIRST®- Testosterone MC in Moisturizing Cream Base Compounding Kit components have a three-year expiration date.** Based on real time controlled room temperature and humidity testing, *compounded* FIRST®- Testosterone MC in Moisturizing Cream Base is stable for at least six months.**

Each lot of FIRST®- Testosterone MC solution meets USP Microbial Limit Tests <61>** for the absence of USP designated pathogens, as well as not more than 100 CFU/mL for total bacterial count and for total yeast and mold. FIRST®- Testosterone MC solution also meets USP Antimicrobial Effectiveness Testing <51>**. Antimicrobial effectiveness has been demonstrated in freshly prepared testosterone propionate solution samples and testosterone propionate solution samples stored at accelerated ICH storage conditions (40±2°C/75%RH).

For external use only. Avoid contact with eyes. Keep container tightly closed. Keep out of the reach of children. Compounded product, as dispensed, is ***stable for at least 180 days*** at room temperature.

* Certificate of analysis on file

** Data and documentation on file

℞ ONLY

Revised: April 2007

U.S. Patent No. 6,708,822 B1

Additional U.S. Patent Pending

Distributed By:

CUTISPHARMA, INC.

SMART PRODUCTS FOR SMART PEOPLE™

Beverly, MA 01915, USA www.cutispharma.com

FIRST®- Hydrocortisone ℞

10% Hydrocortisone in Ultrasound Gel Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

Each FIRST®- Hydrocortisone in Ultrasound Gel Compounding Kit contains 6 grams of micronized hydrocortisone USP in a suspension* (total weight: 24 g) with propylene glycol USP and simethicone USP.

FIRST®- Hydrocortisone in Ultrasound Gel Compounding Kit also contains 36 grams of ultrasound gel for topical use. When compounded, the final product provides an homogeneous gel cream containing 10% hydrocortisone.

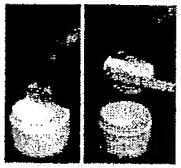
How Supplied and Compounding Directions

Size (Net Weight)	60 grams
NDC#	65628-010-01
Hydrocortisone Suspension	24 grams
Ultrasound Gel	36 grams

TO THE PHARMACIST

Everything you need to make this ℞ is included...

1. FIRST®- Hydrocortisone in Ultrasound Gel Compounding Kit contains pre-weighed hydrocortisone suspension in a mixture of propylene glycol and simethicone in a mixing jar, pre-weighed ultrasound gel, and a stirrer.



2. Prior to dispensing, carefully peel back the inner foil seal of the jar containing the hydrocortisone suspension. Incorporate all of the hydrocortisone suspension, including any material on the inner seal.

3. Important - Empty the ultrasound gel into the hydrocortisone suspension by thoroughly squeezing the entire pouch.

4. Stir until homogeneous in appearance (2 to 3 minutes).

Prior to compounding, store FIRST®- Hydrocortisone in Ultrasound Gel Compounding Kit at room temperature between 15°-30°C (59°-86°F). Also store final formulation at room temperature, 15°-30°C (59°-86°F).

FIRST®- Hydrocortisone in Ultrasound Gel Compounding Kit components have a two-year expiration date.** Based on real time controlled room temperature and humidity testing, *compounded* FIRST®- Hydrocortisone in Ultrasound Gel is stable for at least six months.**

Each lot of FIRST®- Hydrocortisone suspension meets USP Microbial Limit Tests <61>** for the absence of USP designated pathogens, as well as not more than 100 CFU/mL for total bacterial count and for total yeast and mold. FIRST®- Hydrocortisone suspension also meets USP Antimicrobial Effectiveness Testing <51>**. Antimicrobial effectiveness has been demonstrated in freshly prepared hydrocortisone suspension samples and hydrocortisone suspension samples stored at accelerated ICH storage conditions (40±2°C/75%RH).

For external use only. Avoid contact with eyes. Keep container tightly closed. Keep out of the reach of children. Compounded product, as dispensed, is ***stable for at least 180 days*** at room temperature.

* Certificate of analysis on file

** Data and documentation on file

℞ only

Revised: January 2008

U.S. Patent No. 6,708,822 B1

Additional U.S. Patent Pending

Distributed By:

CUTISPHARMA, INC.

SMART PRODUCTS FOR SMART PEOPLE™

Woburn, MA 01801, USA www.cutispharma.com

FIRST®- Mouthwash BLM R

Diphenhydramine HCl, Lidocaine HCl, Aluminum Hydroxide, Magnesium Hydroxide, and Simethicone Compounding Kit

FOR PRESCRIPTION COMPOUNDING ONLY

DESCRIPTION

Each FIRST®- Mouthwash BLM Compounding Kit is comprised of 0.2 grams of diphenhydramine hydrochloride powder USP and 1.6 grams of lidocaine hydrochloride powder USP for oral use.* FIRST®- Mouthwash BLM Compounding Kit also contains a 236 mL suspension containing 3.15 grams of aluminum hydroxide USP (equivalent to dried gel USP), 3.15 grams of magnesium hydroxide USP, and 0.315 grams of simethicone USP with benzyl alcohol, butylparaben, flavor, hydroxyethylcellulose, propylparaben, purified water, saccharin sodium, sorbitol solution, D&C red #28, and FD&C red #40.* When compounded, the final product provides an homogeneous suspension containing diphenhydramine hydrochloride, lidocaine hydrochloride, and aluminum hydroxide, magnesium hydroxide, and simethicone comparable to the active ingredients (Benadryl®, Lidocaine HCl 2% Viscous, Maalox® 1:1:1) contained in *Magic Mouthwash*.**

How Supplied and Compounding Directions

Size	8 FL OZ (237 mL)
NDC#	65628-050-01
Diphenhydramine HCl	0.2 g
Lidocaine HCl	1.6 g
FIRST®- Mouthwash Suspension	236 mL

TO THE PHARMACIST

Everything you need to make this R is included...

1. FIRST®-Mouthwash BLM Compounding Kit contains premeasured diphenhydramine hydrochloride powder, lidocaine hydrochloride powder and mouthwash suspension (aluminum hydroxide, magnesium hydroxide, simethicone plus inactive ingredients).

2. Important – Before dispensing, tap the top and bottom of the bottle containing diphenhydramine hydrochloride to loosen the powder and remove the cap. Empty the diphenhydramine hydrochloride powder into the bottle containing the mouthwash liquid suspension. Likewise, tap the top and bottom of the bottle containing lidocaine hydrochloride to loosen the powder and remove the cap. Empty the lidocaine hydrochloride powder into the bottle containing the mouthwash liquid suspension. The appropriate quantities of diphenhydramine hydrochloride powder and lidocaine hydrochloride powder have been packaged in each bottle to deliver the required dosage of each drug. Residual quantities remaining in the bottles after emptying need not be rinsed out.

3. Close the bottle and shake for 20 to 30 seconds. Instruct the patient to shake bottle well before each use.

Prior to compounding, store FIRST®- Mouthwash BLM Compounding Kit at room temperature between 15°-30°C (59°-86°F) [see USP]. Also store final formulation at room temperature, 15°-30°C (59°-86°F).

FIRST®- Mouthwash BLM Compounding Kit components have a two-year expiration date.*** Based on real time controlled room temperature and humidity testing, *compounded* FIRST®- Mouthwash BLM Compounding Kit is stable for at least six months.***

FIRST®- Mouthwash suspension meets the requirements for total aerobic microbial count of not more than 100 CFU/mL, as well as for the absence of USP designated pathogens (*Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, and Salmonella ssp.*) when tested as described in the USP <61> Microbial Limit Tests.*** Both freshly prepared FIRST®- Mouthwash suspension samples and FIRST®- Mouthwash suspension samples which have been stored at accelerated ICH storage conditions (40±2°C/75%RH) meet the USP <51> requirements for Antimicrobial Effectiveness Testing, Category 4.***

For oral use only. Avoid contact with eyes. Keep container tightly closed. Keep out of the reach of children. Protect from light. Protect from freezing. Compounded product, as dispensed, is ***stable for at least 180 days*** at room temperature.

* Certificate of analysis on file

** This product is not manufactured by Pfizer, Inc., manufacturer of Benadryl® or by Novartis Consumer Health, Inc. manufacturer of Maalox®

*** Data and documentation on file

R ONLY

Revised: February 2008

U.S. Patent No. 6,708,822 B1

Additional U.S. Patent Pending

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CUTISPHARMA, INC.

SMART PRODUCTS FOR SMART PEOPLE™

Woburn, MA 01801, USA www.cutispharma.com

ORAL SUSPENSION

CutisPharma

WHOLESALERS FIRST® Unit-of-Use Prescription Compounding Kits

	FIRST— Progesterone VGS 25	FIRST— Progesterone VGS 50	FIRST— Progesterone VGS 100	FIRST— Progesterone VGS 200	FIRST— Progesterone VGS 400	
NDC #	65628-060-01	65628-061-01	65628-062-01	65628-063-01	65628-064-01	
Wholesaler						**Website**
ABC	425905	334122	334161	801295	425855	www.amerisourcebergen.com
Anda	---	390751	390752	---	---	www.andameds.com
Bellco Drug Corp.	---	150033	150041	150050	---	www.bellcoonline.com
Cardinal Health	3772746	3627783	3627817	3689163	3772738	www.cardinal.com
CVS	---	---	---	---	---	---
Dakota Drug	---	---	---	---	---	www.dakdrug.com
DIK Drug Co	---	---	---	---	---	www.dikdrug.com
DMS	---	498500	---	---	---	www.dmspharma.com
H.D. Smith Wholesale	---	172-1661	174-7070	202-5005	---	www.hdsmith.com
Kinray	---	384-107	260-919	261-214	255-927	www.kinray.com
McKesson Drug	1862473	1322189	1321314	1953108	1864537	www.mckesson.com
Morris & Dickson	---	---	---	---	---	www.morrisdickson.com
N.C. Mutual	---	---	478628	---	---	www.mutualdrug.com
Rite Aid	65628-060-01	65628-061-01	65628-062-01	65628-063-01	65628-064-01	---
Rochester Drug Co.	10206993	10207009	10207017	10207025	10207033	www.rdcdrug.com
Smith Drug Co	---	08480	---	---	---	www.smithdrug.com
Value Drug	---	410134	---	---	---	www.valuedrugco.com
Walgreens	---	603869	603870	---	---	---

	FIRST— Hydrocortisone 10%	FIRST— Mouthwash BLM	FIRST— BXN Mouthwash	FIRST— Testosterone 2%	FIRST— Testosterone MC 2%	
NDC #	65628-010-01	65628-050-01	65628-051-01	65628-020-01	65628-021-01	
Wholesaler						**Website**
ABC	846337	034987	011-643	846444	670327	www.amerisourcebergen.com
Anda	390747	610485	---	201152	201153	www.andameds.com
Bellco Drug Corp.	150009	151415	---	150017	150025	www.bellcoonline.com
Cardinal Health	3013059	3619210	424-5163	3013067	3420635	www.cardinal.com
CVS	---	335462	---	---	---	---
Dakota Drug	---	648725	---	646554	---	www.dakdrug.com
DIK Drug Co.	388637	388652	---	---	975250	www.dikdrug.com
DMS	---	---	---	---	946-140	www.dmspharma.com
H.D. Smith Wholesale	135-6062	170-4261	2290856	144-3944	144-3936	www.hdsmith.com
Kinray	642033	897454	407-346	642041	714618	www.kinray.com
McKesson Drug	2702348	1287119	1275361	2702470	2741056	www.mckesson.com
Morris & Dickson	407999	628750	016717	408005	449256	www.morrisdickson.com
N.C. Mutual	---	456459	---	328740	347625	www.mutualdrug.com
Rite Aid	65628-010-01	65628-050-01	---	65628-020-01	65628-021-01	---
Rochester Drug Co.	10206977	10206985	---	10206951	10206969	www.rdcdrug.com
Smith Drug Co.	---	39-7992	---	29-7895	42-5900	www.smithdrug.com
Value Drug	166587	392324	---	166579	219865	www.valuedrugco.com
Walgreens	603851	603868	---	603825	603824	---

RX/News

Compounding Elevates Role of Pharmacist

NEW YORK — Compounding is bringing pharmacy back to the future.

In doing so, the process is elevating the profession while gratifying patients, note practitioners. Compounding pharmacists customize medications to narrow specifications from prescribers, enhancing care by meeting patient needs that cannot be fulfilled with mass-produced pharmaceuticals.

"That was the pharmacist's role 150 years ago," says Mike Monske, business development manager at Pharmaca Integrative Pharmacy. "We were to mix and make formulas according to a prescriber's orders. Compounding gives us a much greater role in patient care and interaction with prescribers. It adds another dynamic to pharmacy. It reinforces our ability to talk with patients and prescribers and do what's best for the patient."

"We've come back to the mortar and pestle and brought it into the 21st century," notes Peter Koshland, director of pharmacy and compounding for Elephant Pharm. Instead of being ground and mixed by hand, most compounded drugs are made with sophisticated micronizing and homogenizing equipment that precisely tailors medications and streamlines production, he says.

An estimated 30 million retail and hospital outpatient prescriptions are compounded annually in the United States. About 1% of all prescriptions are compounded, and the U.S. market alone for compounding, at the consumer level, represents an estimated $1 billion a year.

Compounding serves a broad spectrum of prescribers, from oncologists to veterinarians. A topical preparation may be sought for a cancer patient who cannot swallow. Pediatric uses are common, often for chronic conditions for which adult dosages are excessive and adult delivery forms are impractical, while the Women's Health Initiative study has led to widespread demand for compounded bioidentical hormone replacement therapy.

Analgesia is another area suitable for compounders, who can create topical preparations with such medications as morphine or ibuprofen that can be applied directly to the painful area with reduced side effects.

Compounding is a time-consuming process — preparing a medication can take from minutes to two days — and can be costly to get into. Start-up compounding pharmacies may need expensive machinery and training costing up to $10,000.

A way around these challenges is to use compounding kits, such as CutisPharma Inc.'s unit-of-use kits. These preweighed/premeasured, ready to go compounding kits are user-friendly at the bench level, save considerable amounts of pharmacists' time, facilitate third-party reimbursements with a single NDC number for the entire kit and can be compounded while the patient waits, increasing customer satisfaction and eliminating the need for an extra trip to the store.

CutisPharma says it recently established a strategic collaboration with Rite Aid Corp. in which the drug chain will make available FIRST unit-of-use compounding kits to its 5,000-plus stores nationwide through Rite Aid distribution centers.

For the two Davies Pharmacy units in Canton and North Canton, Ohio, which have a reputation for either having or being able to make whatever a patient needs, FIRST kits are invaluable, says owner Steve Fettman.

"We stock everything that CutisPharma makes," he notes. And every time Fettman talks to CutisPharma chairman and chief executive officer Indu Muni, "we talk about other things that we're compounding" for which kits would be valuable for Davies and other pharmacies," he says.

There is an ob-gyn office behind the Canton outlet that regularly prescribes progesterone suppositories for pregnant women, and the FIRST kit for those drugs ensures that the pharmacy has a steady supply. "Even if we're out of stock it doesn't take long to make them up," says Fettman. "It's a great time saver."

Having the kits' premeasured ingredients allows technicians to compound drugs with pharmacists overseeing every step, Fettman points out. The upshot is the assurance that patients at Davies' two Good Neighbor pharmacies are getting "a good-quality product," he notes.

The uniformity of the kits and products results in uniform third-party reimbursement. Insurance companies don't have to question preparation time and know exactly what the patient is getting, Fettman says. And preparation time is "negligible," compared to what it was when Davies had to compound from scratch.

CutisPharma developed the progesterone suppository kits after Fettman discussed their need with Muni. Fettman says he now looks forward "to new kits coming out."

Keith Cook, vice president of clinical operations at Medicine Shoppe International Inc. (MSI), says: "The beauty of [CutisPharma's] offering is that it allows noncompounding pharmacies to accept commonly compounded scripts."

Several Medicine Shoppe and Medi-Cap pharmacies use CutisPharma kits, he adds. "They can just order a kit, put it together, dispense the drug and not have to turn that customer away. A lot of pharmacies find it easier to do that than spend all the money and go through the training required to get into compounding. CutisPharma has done all that work for you."

Regardless of the level of compounding a pharmacy chooses, the practice can be profitable. Most pharmacy benefits managers are highly receptive to covering compounding, says Cook, who estimates that more than 500 MSI units practice some form of compounding.

For its part, Walgreen Co. operates 340 Compound Centers of Excellence nationwide. The centers use state-of-the-art equipment, and their pharmacists attend an accredited training program and receive continued support.

An Alternative to Standard HRT Gains Momentum

NEW YORK — Among the drivers of compounding has been the pursuit of a safe treatment for menopause symptoms.

Traditional hormone replacement therapy (HRT) came under fire in 2002 when it was linked to an increased rate of heart attack, stroke and breast cancer by the Women's Health Initiative (WHI), a federal study of 16,000 women. The discovery of the linkage led to the abrupt halt of the study.

An alternative to traditional HRT pills, which combines horse estrogen and a synthetic progesterone in a uniform dosage, is a dose of compounded bioidentical hormones. This approach has gained fierce adherents, including actress Suzanne Somers and Oprah Winfrey, who recently featured the topic on her show.

Winfrey, who turned 55 in January, says bioidentical hormones have significantly improved her health. She writes in February's edition of *O, The Oprah Magazine* that she felt "out of kilter" before getting a prescription for bioidentical estrogen. After one day on the prescription, "I felt the veil lift," Winfrey writes. "After three days, the sky was bluer, my brain was no longer fuzzy, my memory was sharper. I was literally singing and had a skip in my step."

Peter Koshland, director of pharmacy and compounding at Elephant Pharm, says the WHI "turned the conventional wisdom about how to treat menopausal symptoms on its head." That led to a lot of confusion, with many women stopping treatment altogether and suffering through hot flashes, sleep disorders, vaginal dryness and other symptoms.

The use of bioidentical hormones had been around for decades but was "lost in the shouting," says Koshland. Bioidentical hormones, though synthesized from plants, are chemically identical to human hormones, he notes.

And because compounded treatments are based on a woman's individual profile — determined, usually, by a saliva test — it gives her the balance of hormonal actions she needs, Koshland points out. Bioidentical hormones provide the lowest possible doses for symptoms. They address quality-of-life issues, avoiding the grand claims of HRT to prevent disease and prolong life, he adds.

"It's a more cautious approach that uses more knowledge of physiology than before, when everyone just kind of bought what everyone else was using," Koshland comments.

Criticism of bioidentical hormones has centered on the lack of double-blind placebo-controlled tests of their safety and efficacy. A year ago the Food and Drug Administration sent letters warning seven pharmacy operations that beneficial claims for bioidentical hormones were unsupported by medical evidence and were considered false and misleading by the agency. That action, however, led tens of thousands of women to write to Congress defending bioidentical hormones, and to the introduction of House and Senate resolutions calling for the FDA to reverse its course.

Koshland says bioidentical hormones have been used in Europe for more than 50 years, and their safety in low doses is well documented. "For me it's the best option out there," he remarks, adding that their use requires good communication with patients. "We want to educate women so they can be partners in this treatment."

Patent Awarded to CutisPharma

WOBURN, Mass. — A patent for a container and kit for the preparation, storage and dispensing of compounded suppositories has been granted to CutisPharma Inc.

"By its very nature, the process of compounding suppositories is cumbersome, time-consuming and, in general, without adequate compensation," states Dr. Indu Muni, founder, chairman and chief executive officer of CutisPharma Inc. "Our container [suppository mold] and the method for suppository compounding is user-friendly and time-saving for a pharmacy."

Muni adds that CutisPharma's suppository mold is also customer-friendly, because the take-home molds are especially designed not only to maintain the integrity of each suppository once compounded but also to provide convenient dispensing tools.

'The method for suppository compounding is user-friendly and time-saving for a pharmacy'

The CutisPharma FIRST Progesterone Vaginal Suppository Unit-of-Use Prescription Compounding Kit product line, which uses the patented container, is currently available.

The line includes FIRST Progesterone VGS 25, 50, 100, 200 and 400, representing various strengths (milligrams). The kits are made for a single patient and include preweighed progesterone and the patented disposable container/mold for preparation, storage and dispensing of the suppositories.

A single NDC number assigned to the entire kit aids the third-party reimbursement process and reduces audit-related adjustments. FIRST kits also comply with U.S. Pharmacopeia regulations.

The patented container and kit, and the method, will be used for future suppository compounding kits, including boric acid and morphine.

CutisPharma estimates that more than 1.5 million progesterone suppository prescriptions are written in the United States annually, representing a potential of nearly $100 million at the retail level. The kit provides a pharmacy with an easy entry into the market.

Local pharmacist vies for $50,000 award

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KAREN LONGWELL

Homegrown ideas could change the face of industry in Saskatchewan, says Prince Albert pharmacist Steve Mamchur.

Mamchur is one of five budding entrepreneurs up for a $50,000 award from the University of Saskatchewan in the Bio Venture Challenge. The challenge offers intensive coaching and mentorship to refine business plans. At the end of the summer the entrepreneur with the best plan will receive the award.

Mamchur has developed a prescription mixing process that could help women who require hormone replacement therapy. Bio-identical hormone therapy has been made famous by actress Suzanne Somers, who wrote books about how the hormones relieved her menopausal symptoms.

Topics : **University of Saskatchewan , Prince Albert , Saskatchewan Agriculture , Saskatchewan , Canada , Toronto**

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Mamchur hopes to form a company that will manufacture the hormone replacement solution.

"My vision is to start this company in Saskatchewan and basically prove to the rest of Canada that we can do some amazing things in Saskatchewan with

home-grown ideas - we don't have to take our ideas to Toronto or Calgary or somewhere like that."

Right now women who require hormone replacement therapy are usually on an oral treatment and that is usually a synthetic hormone, Mamchur says. This type of hormone can be hard on your body because it is taken in higher doses and the hormone is different from what your body normally produces.

Mamchur's product provides pharmacists with a simpler way to mix topical cream that is already on the market but hard for many women to get. To make the cream, pharmacies need a dedicated space, equipment to weigh the various powders, and protective gear.

Every pharmacy will be able to use the liquid solution Mamchur has developed. But this a flagship product; there will be future products utilizing the same idea.

Mamchur chose to do this one first because of the huge market of the baby-boomer generation.

The $50,000 award would make it easier for Mamchur to get his business venture started.

The University of Saskatchewan's Bio Venture Challenge is a joint initiative with Saskatchewan Agriculture and Food. It is open to recent U of S graduates who are younger than 35 years old.